I. Amendments to the Claims

This listing of claims shall replace all prior versions, and listings, of claims in the application.

Listing of Claims

Claim 1. (Currently amended) An oral dosage form comprising (i) an opioid agonist in releasable form, ~~and~~ (ii) particles of ~~a therapeutically active agent consisting essentially of~~ a sequestered opioid antagonist, ~~which is substantially not released when the dosage form is administered intact~~ and (iii) a sequestering material separating the antagonist from the agonist and substantially preventing the release of the antagonist from the dosage form which has been administered intact such that ~~the~~ a ratio of ~~the~~ an amount of the antagonist released from ~~said~~ the dosage form after tampering to ~~the~~ an amount of ~~said~~ the antagonist released from ~~said~~ the intact dosage form is about 4:1 or greater, based on the in-vitro dissolution ~~at 1 hour~~ of ~~said~~ the dosage form at 1 hour in 900 ml of Simulated Gastric Fluid using a USP Type II (paddle) apparatus at 75 rpm at 37 degrees C;
wherein ~~said~~ the agonist and the particles ~~of the sequestered opioid antagonist~~ are interdispersed and are not isolated from each other in two distinct layers.

Claim 2. (Currently amended) An oral dosage form comprising (i) an opioid agonist in releasable form, ~~and~~ (ii) particles of ~~a therapeutically active agent consisting essentially of~~ a sequestered opioid antagonist ~~which is substantially not released when the dosage form is administered intact~~, and (iii) a sequestering material separating the antagonist from the agonist and substantially preventing the release of the antagonist from the dosage form which has been administered intact such that ~~the~~ a ratio of ~~the~~ an amount of the antagonist released from ~~said~~ the dosage form after tampering to ~~the~~ an amount of ~~said~~ the antagonist released from ~~said~~ the intact dosage form is about 4:1 or greater, based on the in-vitro dissolution of the dosage form at 1 hour ~~of said dosage~~

~~form~~ in 900 ml of Simulated Gastric Fluid using a USP Type II (paddle) apparatus at 75 rpm at 37 degrees C;
wherein ~~said~~ the particles ~~of the sequestered opioid antagonist~~ are individually coated with ~~a~~ the sequestering material ~~which substantially prevents release of the antagonist~~.

Claim 3. (Currently amended) An oral dosage form comprising (i) an opioid agonist in releasable form, ~~and~~ (ii) particles ~~of a therapeutically active agent consisting essentially~~ of a sequestered opioid antagonist, ~~which is substantially not released when the dosage form is administered intact, such that~~ and (iii) a sequestering material, wherein a ~~the~~ ratio of ~~the~~ an amount of the antagonist released from ~~said~~ the dosage form after tampering to ~~the~~ an amount of ~~said~~ the antagonist released from ~~said~~ the intact dosage form is about 4:1 or greater, based on the in-vitro dissolution at 1 hour of ~~said~~ the dosage form in 900 ml of Simulated Gastric Fluid using a USP Type II (paddle) apparatus at 75 rpm at 37 degrees C; wherein ~~said~~ the antagonist is dispersed in a matrix comprising ~~a~~ the sequestering material,
and the sequestering material separates the antagonist from the agonist and ~~which~~ substantially prevents the release of the antagonist from the dosage form which has been administered intact.

Claim 4. (Currently amended) An oral dosage form comprising (i) an opioid agonist in releasable form, ~~and~~ (ii) particles of ~~a therapeutically active agent consisting essentially of~~ a sequestered opioid antagonist ~~which is substantially not released~~ and (iii) a sequestering material separating the antagonist from the agonist and substantially preventing the release the antagonist from the dosage form which has been ~~when the dosage form is~~ administered intact, such that ~~the~~ a ratio of ~~the~~ an amount of the antagonist contained in ~~said~~ the intact dosage form to ~~the~~ an amount of ~~said~~ the antagonist released from ~~said~~ the intact dosage form after 1 hour is about 4:1 or greater, based on the in-vitro dissolution at 1 hour of ~~said~~ the dosage form in 900 ml of Simulated Gastric Fluid using a USP Type II (paddle) apparatus at 75 rpm at 37 degrees C; wherein ~~said~~ the agonist and the particles ~~of the sequestered opioid antagonist~~ are interdispersed and are not isolated from each other in two distinct layers.

Claim 5. (Currently amended) An oral dosage form comprising (i) an opioid agonist in a releasable form; ~~and~~ (ii) particles ~~of a therapeutically active agent consisting essentially~~ of a sequestered opioid antagonist; ~~which is substantially not released when the dosage form is administered intact,~~ and (iii) a sequestering material separating the antagonist from the agonist and substantially preventing the release of the antagonist from the dosage form, such that ~~the~~ an amount of the antagonist released from ~~said~~ the intact dosage form after 1 hour is less than an amount bioequivalent to 0.25 mg naltrexone and ~~the~~ an amount of ~~said~~ the antagonist released after 1 hour from ~~said~~ the dosage form after tampering is an amount bioequivalent to 0.25 mg naltrexone or more, ~~said release~~ based on the dissolution at 1 hour of ~~said~~ the dosage form in 900 ml of Simulated Gastric Fluid using a USP Type II (paddle) apparatus at 75 rpm at 37 degrees C, wherein ~~said~~ the agonist and the particles ~~of the sequestered opioid antagonist~~ are interdispersed and are not isolated from each other in two distinct layers.

Claim 6. (Currently amended) An oral dosage form comprising (i) an opioid agonist in a releasable form; ~~and~~ (ii) particles ~~of a therapeutically active agent consisting essentially~~ of a sequestered naltrexone or a pharmaceutically acceptable salt thereof ~~which is substantially not released when the dosage form is administered intact~~, and (iii) a sequestering material separating the naltrexone from the agonist and substantially preventing the release the naltrexone from the dosage form such that ~~the~~ an amount of the naltrexone released from ~~said~~ the intact dosage form after 1 hour is less than 0.25 mg and ~~the~~ an amount of ~~said~~ the naltrexone released after 1 hour from ~~said~~ the dosage form after tampering is 0.25 mg or more, ~~said release~~ based on the dissolution at 1 hour of ~~said~~ the dosage form in 900 ml of Simulated Gastric Fluid using a USP Type II (paddle) apparatus at 75 rpm at 37 degrees C, wherein ~~said~~ the agonist and the particles ~~of the sequestered naltrexone~~ are interdispersed and are not isolated from each other in two distinct layers.

Claim 7. (Currently amended) An oral dosage form comprising (i) a therapeuticically effective dose of an opioid agonist; ~~and~~ (ii) particles ~~of a~~

~~therapeutically active agent consisting essentially~~ of a sequestered opioid antagonist, and (iii) a sequestering material separating the antagonist from the agonist and substantially preventing the release the antagonist from the dosage form such that at 1 hour after oral administration, ~~said~~ the dosage form releases not more than 25% of ~~said~~ the antagonist, ~~said~~ the dosage form providing analgesia and ~~said~~ the released antagonist not affecting analgesic efficacy, wherein ~~said~~ the agonist and the particles ~~of the sequestered antagonist~~ are interdispersed and are not isolated from each other in two distinct layers.

Claim 8. (Currently amended) An oral dosage form comprising: (i) an opioid agonist in a releasable form; and ~~an~~ (ii) particles of ~~a therapeutically active agent consisting essentially of~~ an opioid antagonist in substantially non-releasable form wherein ~~said~~ the particles ~~of the sequestered antagonist is~~ are individually coated with a material that separates the antagonist from the agonist and substantially prevents the release of the antagonist from the dosage form which has been administered intact.

Claim 9. (Currently amended) An oral dosage form comprising: (i) an opioid agonist in a releasable form; and ~~an~~ (ii) particles ~~of a therapeutically active agent consisting essentially~~ of an opioid antagonist in substantially non-releasable form, wherein ~~said~~ the antagonist is dispersed in a matrix comprising a material that separates the antagonist from the agonist and substantially prevents the release of the antagonist from the dosage form which has been administered intact.

Claim 10. (Currently amended) The oral dosage form of claim 1, wherein ~~said~~ the ratio is 10:1 or greater.

Claim 11. (Currently amended) The oral dosage form of claim 1, wherein ~~said~~ the ratio is 50:1 or greater.

Claim 12. (Currently amended) The oral dosage form of claim 1, wherein ~~said~~ the ratio is 100:1 or greater.

Claim 13. (Currently amended) The oral dosage form of claim 6, wherein ~~said~~ the intact dosage form releases at least 0.025 mg naltrexone at 1 hour.

Claim 14. (Currently amended) The oral dosage form of claim 1, wherein ~~said~~ the intact dosage form provides at least an amount of antagonist bioequivalent to 0.025 mg naltrexone at 1 hour.

Claim 15. (Currently amended) The oral dosage form of claim 5, wherein the amount of antagonist released after 1 hour from ~~said~~ the tampered dosage form is an amount bioequivalent to 0.5 mg naltrexone or more.

Claim 16. (Currently amended) The oral dosage form of claim 5, wherein the amount of antagonist released after 1 hour from ~~said~~ the intact dosage form is an amount bioequivalent to 0.125 mg naltrexone or less.

Claim 17. (Currently amended) The oral dosage form of claim 6, wherein the amount of antagonist released after 1 hour from ~~said~~ the tampered dosage form is 0.5 mg naltrexone or more.

Claim 18. (Currently amended) The oral dosage form of claim 6, wherein the amount of antagonist released after 1 hour from ~~said~~ the intact dosage form is 0.125 mg naltrexone or less.

Claim 19. (Original) The oral dosage form of claim 1, wherein the opioid agonist is selected from the group consisting of morphine, hydromorphone, hydrocodone, oxycodone, codeine, levorphanol, meperidine, methadone, oxymorphone, buprenorphine, fentanyl and derivatives thereof, dipipanone, heroin, tramadol, etorphine, dihydroetorphine, butorphanol, levorphanol, pharmaceutically acceptable salts thereof and mixtures thereof.

Claim 20. (Original) The oral dosage form of claim 19, wherein the opioid agonist is selected from the group consisting of oxycodone, hydrocodone and pharmaceutically acceptable salts thereof.

Claim 21. (Original) The oral dosage form of claim 1, wherein the opioid antagonist is selected from the group consisting of naltrexone, naloxone, nalmephene, cyclazocine, levallorphan, pharmaceutically acceptable salts thereof and mixtures thereof.

Claim 22. (Original) The oral dosage form of claim 21, wherein the opioid antagonist is selected from the group consisting of naltrexone, naloxone, nalmephene, pharmaceutically acceptable salts thereof and mixtures thereof.

Claim 23. (Original) The oral dosage form of claim 22, wherein the opioid antagonist comprises naltrexone or a pharmaceutically acceptable salt thereof.

Claim 24. (Currently amended) The oral dosage form of claim 2, wherein the sequestering material comprises a cellulose polymer or an acrylic polymer that is insoluble in the gastrointestinal tract and impermeable to the opioid antagonist contained within the coating.

Claim 25. (Original) The oral dosage form of claim 24, wherein the cellulose polymer is selected from the group consisting of ethylcellulose, cellulose acetate, cellulose propionate, cellulose acetate propionate, cellulose acetate butyrate, cellulose acetate phthalate, and mixtures thereof.

Claim 26. (Original) The oral dosage form of claim 24, wherein the acrylic polymer is selected from the group consisting of acrylic acid and methacrylic acid copolymers, methyl methacrylate copolymers, ethoxyethyl methacrylates, cyanoethyl methacrylate, poly(acrylic acid), poly(methacrylic acid), methacrylic acid alkylamide copolymer, poly(methyl methacrylate), polymethacrylate, poly(methyl methacrylate)

copolymer, polyacrylamide, aminoalkyl methacrylate copolymer, poly(methacrylic acid anhydride), and glycidyl methacrylate copolymers.

Claim 27. (Original) The oral dosage form of claim 1, wherein the dosage form provides sustained-release of the opioid agonist.

Claim 28. (Original) The oral dosage form of claim 27, wherein the dosage form is a sustained-release tablet or a sustained-release capsule.

Claim 29. (Currently amended) The oral dosage form of claim 2, wherein ~~said~~ the particles ~~of the sequestered antagonist~~ are in the form of inert beads coated with ~~said~~ the antagonist and overcoated with ~~said~~ the sequestering material.

Claim 30. (Currently amended) The oral dosage form of claim 2, wherein ~~said~~ the particles o~~f the sequestered antagonist~~ are in the form of a granulation comprising ~~said~~ the antagonist and ~~said~~ the sequestering material.

Claim 31. (Currently amended) The oral dosage form of claim 2, wherein ~~said~~ the particles ~~of the sequestered antagonist~~ are dispersed in a matrix comprising ~~said~~ the ~~opioid~~ agonist.

Claim 32. (Currently amended) The oral dosage form of claim 2, wherein ~~said~~ the particles ~~of the sequestered antagonist~~ are contained in a capsule with ~~said~~ the ~~opioid~~ agonist.

Claim 33. (Currently amended) The oral dosage form of claim 3, wherein ~~said~~ the matrix is in the form of pellets.

Claim 34. (Currently amended) The oral dosage form of claim 33, wherein ~~said~~ the pellets are dispersed in a matrix comprising ~~said opioid~~ the agonist.

Claim 35. (Currently amended) The oral dosage form of claim 33, wherein ~~said~~ the pellets are contained in a capsule with ~~said opioid~~ the agonist.

Claim 36. (Currently amended) The oral dosage form of claim 1, wherein ~~said~~ the tampering is by crushing.

Claim 37. (Currently amended) The oral dosage form of claim 27, wherein ~~said~~ the tampering is in a manner as to obtain an immediate release of ~~said~~ the agonist.

Claim 38. (Currently amended) The oral dosage form of claim 1, wherein ~~said~~ the tampering is to make the agonist available for inappropriate use.

Claim 39. (Currently amended) The oral dosage form of claim 1, wherein ~~said~~ the antagonist does not significantly affect analgesia provided by the agonist.

Claim 40. (Currently amended) A method of decreasing the abuse of an opioid agonist in an oral dosage form, comprising incorporating ~~said~~ the opioid agonist into a dosage form of claim 1.

Claim 41. (Currently amended) A dosage form comprising:

(a) an opioid agonist; ~~and~~

(b) particles ~~of a therapeutically active agent consisting essentially~~ of naltrexone in a substantially non-releasable form; and

(c) a sequestering material;

wherein the agonist and naltrexone are separated by the sequestering material, and the agonist and the particles are at least partially interdispersed.

Claim 42. (Original) The dosage form of claim 41 wherein the opioid agonist is oxycodone, codeine, hydrocodone, hydromorphone, levorphanol, meperidine, methadone, morphine, salts thereof, or mixtures thereof.

Claim 43. (Original) The dosage form of claim 42 wherein the opioid agonist is oxycodone hydrochloride.

Claim 44. (Original) The dosage form of claim 42 wherein the opioid agonist is hydrocodone bitartrate.

Claim 45. (Original) The dosage form of claim 42 wherein the opioid agonist is hydromorphone hydrochloride.

Claim 46. (Original) The dosage form of claim 41 wherein at least part of the naltrexone is in a matrix.

Claim 47. (Original) The dosage form of claim 41 wherein at least part of the naltrexone is in a coated bead.

Claim 48. (Original) The dosage form of claim 41 wherein the naltrexone in a substantially non-releasable form is adapted to release less than 15% by weight of the naltrexone *in vivo* after 36 hours.

Claim 49. (Original) The dosage form of claim 48 wherein the naltrexone in a substantially non-releasable form is adapted to release less than 8% by weight of the naltrexone *in vivo* after 36 hours.

Claim 50. (Original) The dosage form of claim 49 wherein the naltrexone in a substantially non-releasable form is adapted to release less than 1% by weight of the naltrexone *in vivo* after 36 hours.

Claim 51. (Original) The dosage form of claim 41 wherein the naltrexone in a substantially non-releasable form is adapted to release less than 3% by weight of the naltrexone *in vivo* after 1 hour.

Claim 52. (Original) The dosage form of claim 41 wherein the naltrexone in a substantially non-releasable form is adapted to release less than 1.0% by weight of the naltrexone *in vivo* after 1 hour.

Claim 53. (Original) The dosage form of claim 41 wherein the naltrexone in a substantially non-releasable form is adapted to release less than 0.5% by weight of the naltrexone *in vivo* after 1 hour.

Claim 54. (Currently amended) A dosage form comprising:

(a) an opioid agonist; ~~and~~

(b) particles ~~of a therapeutically active agent consisting essentially~~ of an orally-bioavailable opioid antagonist in a substantially non-releasable form; and

(c) a sequestering material separating the antagonist from the agonist.

Claim 55. (Original) The dosage form of claim 54 wherein the agonist and antagonist are at least partially interdispersed.

Claim 56. (Original) The dosage form of claim 54 wherein the orally-bioavailable opioid antagonist is naltrexone, or a salt thereof.

Claim 57. (Original) The dosage form of claim 54 wherein the opioid agonist is oxycodone, codeine, hydrocodone, hydromorphone, levorphanol, meperidine, methadone, morphine, or salts thereof or mixtures thereof.

Claim 58. (Original) The dosage form of claim 54 wherein at least part of the antagonist is in a matrix.

Claim 59. (Original) The dosage form of claim 54 wherein at least part of the antagonist is in a coated bead.

Claim 60. (Cancelled)

Claim 61. (Original) A method of treating pain comprising administering to a human patient a dosage form of claim 1.

Claim 62. (New) The oral dosage form of any of claims 1, 2, 3, 4, 5, 7, 19, 21, 29, 30, 31, 32, 33, or 34, wherein the sequestered antagonist is adapted to release less than 15% by weight of the antagonist within 36 hours after administration of an intact dosage form.

Claim 63. (New) The oral dosage form of any of claims 1, 2, 3, 4, 7, 8, 9, 14, 19, 21, 25, 26, 27, 29, 30, 31, 32, 33, 34, 41, 42, 48, 54, 55, 56, 57, 58, or 59, wherein an amount of the antagonist released from the dosage form which has been administered intact is less than an amount bioequivalent to 0.125 mg of naltrexone, based on the in-vitro dissolution of the dosage form at 1 hour in 900 ml of Simulated Gastric Fluid using a USP Type II (paddle) apparatus at 75 rpm at 37 degrees C.

Claim 64. (New): The oral dosage form of claim 62, wherein an amount of the antagonist released from the dosage form which has been administered intact is less than an amount bioequivalent to 0.125 mg of naltrexone, based on the in-vitro dissolution of the dosage form at 1 hour in 900 ml of Simulated Gastric Fluid using a USP Type II (paddle) apparatus at 75 rpm at 37 degrees C.